REMARKS

Claims 1-11, 14-25, 28-35, 44, 45, and 69-84 are pending in the application. Claims 1, 6, 7, 8, 10, 11, 17, 18, 19, 20, 21, 23, 25, 28, 29, 69, 70, and 78 are currently amended. Claims 79-84 are new claims.

Applicant's attorney recently participated in a telephonic interview with Examiner Patterson who is responsible for application serial number 09/917,383. Examiner Patterson believes that the claims of these two applications should be rejected for obviousness-type double patenting because the sequences are the same. Applicant's attorney wishes to bring this to the present attention of Examiner Rao because the sequences should be different. The '383 application addresses different domains including GH6 and GH12 domains, not the GH48 domain of this application. This has been checked and confirmed in the submitted sequence listings themselves. Perhaps the accompanying sequence submission will resolve this issue.

Claim 70 has been amended to delete the word "substantially," as suggested by the Office to overcome the 35 U.S.C. §112 second paragraph rejection of claims 70-74. Claims 1 and 70 have also been amended to delete the word "thermostable." The remaining amendments to claims 6, 7, 8, 10, 11, 17, 18, 19, 20, 21, 23, 25, 28, 29, 69, 70, and 78 are made for various reasons including changes of dependencies and clarification of grammatical issues.

The Conclusion on page 11 of the current Office Action states that none of the claims are presently allowable; however, neither does the Office present a formal rejection of claims 6-11. New claims 79-84 have been added to restate the subject matter of claims 6-9 with slight differences in scope. We respectfully observe that these claims

6-11 and 75-78 identify with specificity the particular sequences including SEQ ID NOS. 4, 5 and 7. Claim 10 is an independent claim that has not been formally rejected, but is also not found to be allowable. Applicant's attorney respectfully solicits an indication that these claims are allowable.

Sequence Compliance

Applicant's attorney resubmits herewith a paper copy of the sequence listing along with a computer-readable disk.

Claim Objections

Claim 11 has been amended to recite more clearly SEQ ID NO. 2 as a nucleotide sequence.

Claim Rejections—35 U.S.C. §112

Claims 1-5, 14-25, 28-35, 44, 45, and 69-74 stand rejected under 35 U.S.C. §112, first paragraph for nonenablement. Examiner has indicated that Claims 6-10 and 78 are allowable if rewritten as independent claims. In the nonenablement rejection, the Examiner asserts that the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of Gux1 polypeptides broadly encompassed by the claims. The Examiner also reasons that because it is not routine in the art to screen for multiple substitutions, Applicants claimed invention requires one of ordinary skills to engage in undue experimentation achieve what is claimed. Applicant respectfully disagrees.

As the court in *In re Wands* pointed out, enablement is not precluded by the necessity for some experimentation such as routine screening. 858 F.2d 731, 8 USPQ2d

1400. No exact numerical standard has been fixed by the courts, but the "amount of required experimentation must, however, be reasonable." *White Consol. Indus.*, 713 F.2d at 791, 218 USPQ at 963. The inquiry is not whether the endeavor is routinely taken in the art. Rather, the inquiry is whether the disclosure provides sufficient guidance so that one of skill in the art would be able to achieve what is claimed using standard or routine techniques in the field.

In that regard, the present application provides not only suggestions to modify amino residues on the Gux1 peptide, but also specific directions as to what regions of the protein may be more conserved than the others. For example, Table 3 shows residues that are conserved among enzymes from the same family. See page 34 of the Specification. Lines 10 to 24 of page 19 provides guidelines on what residues are preferred for substituting a naturally occurring ones. Lines 25 to 30 of page 17 further provides how the activity of the mutated protein can be tested after the substitution. General methodology for making the mutations or for creating the tagged or heterologous peptides is also outlined on pages 19-21. The only instruction not included is details on how to perform the mutagenesis. However, as DeGrado et al. pointed out, site-directed mutagenesis was standard technique for determining which residues in a protein are essential for folding or function, even in the year 1989. See DeGrado et al., Protein Design, a Minimalist Approach, Science, 1989, 243:622-28.

With all due respect, the Office is simply wrong in assuming that the specification fails to disclose a representative number of species. This determination is made from the perspective of ordinary skill. The specification provides Table 3 and a discussion of site-

directed mutagenesis. Thus, enablement of the genus-level claim does exist from the perspective of ordinary skill. This exists at least from the perspective of Table 3 and that those of ordinary skill would be able to use site-directed mutagenesis to make conservative substitutions on this basis.

Applicants have also amended some existing claims and have added new claims that are commensurate with the scope of enablement provided by the specification. Claim 1 and its dependant claims have been amended to recite the conserved sequence of GH48 catalytic domain. Claim 1, in its current form, encompasses peptides that are either disclosed or taught with sufficient guidance in the specification. Claim 6 has also been rewritten as an independent claim. Claims 7 and 8 depends from Claim 6. Claim 10 is an independent claim, from which Claim 11 depends. All claims, as currently amended, recite the limitation of SEQ ID NO. 1, 3, 4, 5, 6 or 7, which are enabled according to the Office Action. Therefore, Applicants respectfully request withdrawal of the rejections based on 35 U.S.C. §112 for nonenablement.

Claims 1-5, 22-25, 28-35, 44-45 and 69-74 stand rejected under 35 U.S.C. §112 for lack of possession. The Examiner maintains that while the CAZy databases provide guidance for other practitioners to construct variants of the Gux1 peptide by modifying the structure of the three domains, no functions of the variants are provided in those databases. However, Examiner fails to recognize that the functional test for these variants and the manner of making them is well within the perspective of skill and, further, the level of required experimentation is not undue for this art. The Federal Circuit acknowledges confusion between the respective enablement and possession

requirements in context of written descriptions, but also that the standards are related and intertwined:

> There appears to be some confusion in our decisions concerning the extent to which the "written description" requirement is separate and distinct from the enablement requirement. . . .
>
> . . .This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116-1117 (Fed. Cir 1991).

As to written description, the Office observes Applicant's citation of *Enzio Biochem* in a previous response, but chooses to distinguish the application of *Enzio* on the specific facts of this case. The case actually cited in the prior response cited was *Amgen*, but the quoted passage did rely upon *Enzio*. The issue of written description devolves to Office allegations that the application discloses a species but claims a genus. The Office now agrees that a genus claim may be supported by a representative number of disclosed species--not all species within a genus need be specifically disclosed. *Amgen* was cited for the principle that it is not necessary to enunciate each and every species encompassed by a genus claim. This is a matter of law—Applicant is not required to disclose each and every one of 132,000 combinations, and it does suffice that Applicant has presented a structural rationale, for example, by showing the conserved residues in Table 3 on page 34 of the specification.

We fail to understand how the Office distinguishes the Enzio/Amgen premise of law on the facts of this case. The guidance to use combinations of domain families leads

inevitably to a large number of combinations, but this is routine for this art.. Dr. Himmel's declaration provides evidence that something like 132,000 combinations of structure are obtainable within the level of ordinary skill from the broad guidance and knowledge imparted by the present Specification. Surely this is a representative number of species to support a genus claim from the perspective of ordinary skill.

The Office has merely repeated a prior rejection without addressing these points. Therefore, we respectfully traverse the 'possession of the invention' rejection and request it to be withdrawn.

Again, the Office refers to written description guidelines located generally at www.uspto.gov. We are unable to find the specific guidelines at this location and again request the Office to particularly identify a citation if they are relevant to this prosecution. The Office should point particularly to the guidelines in question.

Claims 28-35, 44, and 45 stand rejected under 35 U.S.C. §112 first paragraph. This rejection is stated because the claims recite identity with specifically disclosed sequences ranging from 70% to 90% identity. The Office asserts that there is substantial variation within the claimed genus, so one must describe a representative number of species in support of the genus. The representative number of species must relate functionality to relevant identifying characteristics, such as structural, physical, or chemical properties. This is precisely what Applicant has done, for example, beginning at line 12 on page 19 of the Specification where there is a suggestion to make conservative substitutions of like-functioning residues, and on page 20 where fusion proteins are discussed, so it cannot be said that such guidance is absent.

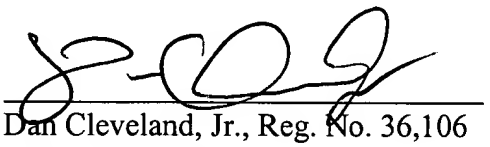
The Office further alleges that claims 8-35, 44, and 45 read upon a wide variety of functionally unrelated compositions and that the modified peptide sequences would have a diverse range of functionalities. We fail to understand the relevancy of the Office position, because a wide range of utilities are also disclosed and it is permissible for a species or genus of composition to have a wide range of functionality. A selection of useful modified peptides may be made based upon the claimed sequences, for example, as recited in the paragraph beginning at line 23 on page 20. Even if the modification of a peptide sequence results in rendering the peptide nonfunctional for its natural purpose, such peptides also have utility, for example, in fully characterizing the domain or in selectively blocking activity of the peptide in a competitive assay, which may be performed according to the last paragraph on page 17 of the Specification.

The Office rejects claims 1-5, 22-25 and 69-74 for including new matter. This is essentially stated on the same basis as above, i.e., because "[n]o description has been provided of even a representative number of polypeptide sequences encompassed by the [genus] claim." The Office reiterates "**when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.**" Actually, the Examiner incorrectly adopts as a *per se* rule what is only one way of making the requisite showing. Another way to do this is to adopt a structural rationale, for example, as Applicant has disclosed in Table 3. This is understood from the perspective of skill as encompassing a genus of variations, and Dr. Himmels's declaration is provided to show this is true.

For the reasons stated above, Applicant's attorney respectfully solicits allowance of all the claims.

Applicant's attorney respectfully solicits a Notice of Allowance in this application. The Commissioner is authorized to charge any additionally required fees to deposit account 12-0600. Should the Examiner have any questions, comments, or suggestions that would expedite the prosecution of the present case to allowance, Applicants' representative, Paul White, earnestly requests a telephone call at (303) 384-7575.

Respectfully submitted



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